



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-0011]

Establish a Patient-Based Registry to Evaluate the Association of Gadolinium Based Contrast Agents Exposure and Nephrogenic Systemic Fibrosis

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of grant funds for the support of the development of a patient-based registry to evaluate the association of gadolinium based contrast agents (GBCAs) exposure and nephrogenic systemic fibrosis (NSF).

The goal of the GBCA project is to study the safety of the GBCAs when used as indicated.

DATES: Important dates are as follows:

1. The application due date is August 1, 2012.
2. The anticipated start date is September 13, 2012.
3. The opening date is July 2, 2012.
4. The expiration date is August, 2, 2012.

ADDRESSES: Submit the paper application to: Vieda Hubbard, Grants Management (HFA-500), 5630 Fishers Lane, Rockville, MD 20857, and a copy to Ira Krefting, Center for Drug Evaluation and Research, Division of Medical Imaging Products, 10903 New Hampshire Ave., Bldg. 22, rm. 2100, Silver Spring, MD 20993. For more information, see section III of the SUPPLEMENTARY INFORMATION section of this notice.

FOR FURTHER INFORMATION AND ADDITIONAL REQUIREMENTS CONTACT:

Ira Krefting,

Center for Drug Evaluation and Research (CDER),

Food and Drug Administration,

10903 New Hampshire Ave.,

Bldg. 22, rm. 2100,

Silver Spring, MD 20993,

301-796 1135,

Email: ira.krefting@fda.hhs.gov; or

Vieda Hubbard,

Office of Acquisitions and Grants Services (HFA-500),

Food and Drug Administration,

5630 Fishers Lane, rm. 2034,

Rockville, MD 20857,

301-827-7177,

Email: vieda.hubbard@fda.hhs.gov.

For more information on this funding opportunity announcement (FOA) and to obtain detailed requirements, please refer to the full FOA located at:

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM311309.pdf>.

SUPPLEMENTARY INFORMATION:

I. Funding Opportunity Description

RFA-FD-12-029

93.103

A. Background

Annually, millions of patients undergo magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) procedures employing GBCAs. Postmarketing data indicate that six of the eight GBCAs approved for use in the United States have been directly implicated in the development of NSF, a newly characterized, potentially fatal systemic fibrotic skin and internal organ condition. Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of GBCA and degree of renal impairment at the time of exposure; imaging patients with severe renal failure appear to be at highest risk. In one, early retrospective study of 370 patients with severe renal failure who received gadodiamide the estimated risk for development of NSF was 4 percent (Ref. 1). In a recent retrospective chart review study by Wang of 52,954 contrast MR examinations with restrictive guidelines for GBCA in patients with renal failure no new cases of NSF were found (Ref. 2).

In addition, the NSF risk appears to vary among the GBCAs. Postmarketing data and corroborating preclinical data that demonstrated a significant, unacceptable NSF risk has led FDA to recently contraindicate Omniscan, Magnevist, and Optimark for patients with acute kidney injury and severe chronic renal failure. The risk of NSF associated with the remaining marketed GBCAs for patients with these kidney conditions is expected to be lower, but is not fully understood. Therefore, there is a public health need to study the risk of NSF associated with the exposure of those remaining marketed GBCAs and to inform the development of

reliable knowledge, practice guidelines, and regulatory processes in relationship to the safety of these agents.

B. Research Objectives

The primary goal of this project is to employ an existing Quality Assurance (QA) registry of patients with renal failure who received GBCAs as the basis for a prospective registry study of the risk of NSF associated with GBCAs among renal patients. Patients already enrolled in this QA registry will be invited to enroll in an outpatient registry to study their risk of NSF. Data from this project will help understand the effect of cumulative dosing of the GBCAs in patients with slow deterioration of renal function as occurs with aging, and the data might also provide further reassurance as to the safety of the GBCAs identified as having minimal association with the risk of NSF by prospectively following patients who have received GBCAs. In addition, the project will also provide data on the occurrence of allergic reactions associated with the GBCA administration. A recent report by Prince suggests an increased risk of allergic reactions with MultiHance (Ref. 3).

The prospective design of this project is important since most previous clinical investigations have been based on chart review or other retrospective data. Implementation of this project may also provide the structure for future prospective investigations of other diseases with an acute phase of hospitalization superimposed on a chronic course.

C. Eligibility Information

This is a sole source cooperative agreement to: University of Pittsburgh Medical Center.

II. Award Information/Funds Available

A. Award Amount

CDER anticipates providing in FY2012 \$250,000 (total costs include direct and indirect costs), for one award subject to availability of funds in support of this project.

B. Length of Support

Support will be 1 year with the possibility of an additional year of noncompetitive support. Continuation beyond the first year will be based on satisfactory performance during the preceding year, receipt of a noncompeting continuation application and subject to the availability of Fiscal Year appropriations.

III. Paper Application, Registration, and Submission Information

To submit a paper application in response to this FOA, applicants should first review the full announcement located at:

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM311309.pdf>. (FDA has verified the Web site addresses throughout this document,

but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the Federal Register.) Persons interested in applying for a grant may obtain an application at:

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM311309.pdf>. For all paper application submissions, the following steps are

required:

- Step 1: Obtain a Dun and Bradstreet (DUNS) Number
- Step 2: Register With Central Contractor Registration
- Step 3: Register With Electronic Research Administration (eRA) Commons

Steps 1 and 2, in detail, can be found at:

http://www07.grants.gov/applicants/organization_registration.jsp. Step 3, in detail, can be found at: <https://commons.era.nih.gov/commons/registration/registrationInstructions.jsp>. After you have followed these steps, submit one paper application to: Vieda Hubbard, Grants Management, Food and Drug Administration, Division of Support and Grants, 5630 Fishers Lane, rm. 1079, HFA 500, Rockville, MD 20857 and a copy to Ira Krefting, Center for Drug Evaluation and Research, Division of Medical Imaging Products, 10903 New Hampshire Ave., Bldg. 22, rm. 2100, Silver Spring, MD 20993.

IV. References

The following references have been placed on display in the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Marckmann, Peter; Skov, Lone; Rossen, Kristian; Dupont, Anders; Damholt, Mette Brimnes; Heaf, James Goya; and Thomsen, Henrik, Journal of the American Society of Nephrology, 17:2359, 2006.
2. Wang, Yingbing; Alkasab, Tarik; Narin, Ozden; Nazarian, Rosalynn; Kaewali, Rathachai, Kaewlai; Kay, Jonathan; and Abujudeh, Hani, Radiology, 260:105, 2011.
3. Prince, Martin; Zhang, Honglei; Zou, Zhitong; Staron, Ronald; and Brill, Paula, American Journal of Radiology, 196(2):W138, 2011.

Dated: July 13, 2012.

Leslie Kux,

Assistant Commissioner for Policy.

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